



General

Guideline Title

Pregnancy outcomes after assisted human reproduction.

Bibliographic Source(s)

Society of Obstetricians and Gynaecologists of Canada, Okun N, Sierra S. Pregnancy outcomes after assisted human reproduction. J Obstet Gynaecol Can. 2014 Jan;36(1):64-83. [176 references] [PubMed](#)

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Allen VM, Wilson RD, Cheung A; Genetics Committee of the Society of Obstetricians and Gynaecologists of Canada (SOGC); Reproductive Endocrinology Infertility Committee of the Society of Obstetricians and Gynaecologists of Canada (SOGC). Pregnancy outcomes after assisted reproductive technology. J Obstet Gynaecol Can. 2006 Mar;28(3):220-50. [117 references]

Recommendations

Major Recommendations

The quality of evidence assessment (I-III) and classification of recommendations (A-E, L) are defined at the end of the "Major Recommendations" field.

Outcomes Associated with Untreated Infertility

Summary Statement

1. There is increasing evidence that infertility or subfertility is an independent risk factor for obstetrical complications and adverse perinatal outcomes, even without the addition of assisted human reproduction (AHR). (II-2)

Outcomes Associated with Male Factor Infertility

Recommendations

1. All men with severe oligozoospermia or azoospermia (sperm count <5 million/hpf) should be offered genetic/clinical counselling, karyotype assessment for chromosomal abnormalities, and Y-chromosome microdeletion testing prior to in vitro fertilization (IVF) with intracytoplasmic sperm injection (ICSI). (II-2A)
2. All men with unexplained obstructive azoospermia should be offered genetic/clinical counseling and genetic testing for cystic fibrosis prior to

Obstetrical, Perinatal, and Long-Term Outcomes Associated with Assisted Reproductive Technology

Multiple Pregnancy and Adverse Obstetrical and Perinatal Outcomes

Recommendations

3. Multiple pregnancy is the most powerful predictive factor for adverse maternal, obstetrical, and perinatal outcomes. Couples should be thoroughly counselled about the significant risks of multiple pregnancies associated with all assisted human reproductive treatments. (II-2A)
4. The benefits and cumulative pregnancy rates of elective single embryo transfer (eSET) support a policy of using this protocol in couples with good prognosis for success, and eSET should be strongly encouraged in this population. (II-2A)
5. To reduce the incidence of multiple pregnancy, health care policies that support public funding for AHR, with regulations promoting best practice regarding eSET, should be strongly encouraged. (II-2A)

Singleton Pregnancies and Perinatal Outcome/Preterm Birth/Low Birth Weight

Recommendations

6. Among singleton pregnancies, assisted reproductive technology (ART) is associated with increased risks of preterm birth and low birth weight infants, and ovulation induction (OI) is associated with an increased risk of low birth weight infants. Until sufficient research has clarified the independent roles of infertility and treatment for infertility, couples should be counselled about the risks associated with treatment. (II-2B) There is a role for closer obstetric surveillance for women who conceive with AHR. (III-L)
7. There is growing evidence that pregnancy outcomes are better for cryopreserved embryos fertilized in vitro than for fresh embryo transfers. This finding supports a policy of eSET for women with a good prognosis (with subsequent use of cryopreserved embryos as necessary), and may reassure women who are considering IVF. (II-2A)
8. Women and couples considering AHR and concerned about perinatal outcomes in singleton pregnancies should be advised that (1) ICSI does not appear to confer increased adverse perinatal or maternal risk over standard IVF, and (2) the use of donor oocytes increases successful pregnancy rates in selected women, but even when accounting for maternal age, can increase the risk of low birth weight and preeclampsia. (II-2B)

Fetal Structural, Chromosomal, and Imprinting Abnormalities Associated with Assisted Human Reproduction

Structural Abnormalities (Malformations, Deformations, and Disruptions)

Recommendations

9. Any ART procedure should be prefaced by a discussion of fetal outcomes and the slight increase in the risk of congenital structural abnormalities, with emphasis on known confounding factors such as infertility and body mass index. (II-2B)
10. In pregnancies achieved by ART, routine anatomic ultrasound for congenital structural abnormalities is recommended between 18 and 22 weeks. (II-2A)

Chromosomal Disorders

Recommendation

11. Pregnancies conceived by ISCI may be at increased risk of chromosomal aberrations, including sex chromosome abnormalities. Diagnostic testing should be offered after appropriate counselling. (II-2A)

Imprinting Disorders

Summary Statement

2. The relative risk for an imprinting phenotype such as Silver-Russell syndrome, Beckwith-Wiedemann syndrome, or Angelman syndrome is increased in the assisted reproduction population, but the actual risk for one of these phenotypes to occur in an assisted pregnancy is estimated to be low, at less than 1 in 5000. The exact biological etiology for this imprinting risk increase is likely heterogeneous and requires more research. (II-2)

Recommendation

12. The possible increased risk for late onset cancer due to gene dysregulation for tumour suppression requires more long-term follow-up

before the true risk can be determined. (III-A)

Preimplantation Genetic Screening

Recommendations

13. The clinical application of preimplantation genetic testing in fertile couples must balance the benefits of avoiding disease transmission with the medical risks and financial burden of IVF. (III-B)
14. Preimplantation screening for aneuploidy is associated with inconsistent findings for improving pregnancy outcomes. Any discussion of preimplantation genetic screening with patients should clarify that there is no adequate information on the long-term effect of embryo single cell biopsy. (I-C)

Definitions:

Quality of Evidence Assessment*

I: Evidence obtained from at least one properly randomized controlled trial

II-1: Evidence from well-designed controlled trials without randomization

II-2: Evidence from well-designed cohort (prospective or retrospective) or case-control studies, preferably from more than one centre or research group

II-3: Evidence obtained from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of treatment with penicillin in the 1940s) could also be included in this category

III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees

*Adapted from the Evaluation of Evidence criteria described in the Canadian Task Force on Preventive Health Care.

Classification of Recommendations[†]

A. There is good evidence to recommend the clinical preventive action

B. There is fair evidence to recommend the clinical preventive action

C. The existing evidence is conflicting and does not allow to make a recommendation for or against use of the clinical preventive action; however, other factors may influence decision-making

D. There is fair evidence to recommend against the clinical preventive action

E. There is good evidence to recommend against the clinical preventive action

L. There is insufficient evidence (in quantity or quality) to make a recommendation; however, other factors may influence decision-making

[†]Adapted from the Classification of Recommendations criteria described in the Canadian Task Force on Preventive Health Care.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Assisted human reproduction (AHR) pregnancies

Guideline Category

Counseling

Management

Risk Assessment

Clinical Specialty

Medical Genetics

Obstetrics and Gynecology

Intended Users

Advanced Practice Nurses

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

- To review the effect of assisted human reproduction (AHR) on perinatal outcomes
- To identify areas requiring further research with regard to birth outcomes and AHR
- To provide guidelines to optimize obstetrical management and counselling of prospective Canadian parents

Target Population

Infertile and subfertile women and men

Interventions and Practices Considered

1. Consideration of infertility or subfertility as an independent risk factor for obstetrical complications and adverse perinatal outcomes
2. Male factor infertility
 - Genetic/clinical counselling
 - Karyotype assessment for chromosomal abnormalities
 - Y-chromosome microdeletion testing
 - Genetic testing for cystic fibrosis
3. Assisted reproductive technology (ART)
 - Counselling on risks of ART (multiple pregnancies, preterm birth, low birth weight)
 - Benefits of elective single embryo transfer (eSET)
 - Consideration of cryopreserved embryos fertilized in vitro vs. fresh embryo transfers
 - Advisement concerning intracytoplasmic sperm injection (ICSI) and use of donor oocytes
4. Assisted human reproduction (AHR) associated fetal structural, chromosomal and imprinting abnormalities
 - Patient counseling on risks of congenital structural abnormalities
 - Routine anatomic ultrasound
 - Risk of chromosomal aberrations and imprinting disorders
 - Long-term follow-up for possible risk of late onset cancer
5. Preimplantation genetic testing
6. Close obstetric surveillance for AHR pregnancies

Major Outcomes Considered

- Obstetrical complications
- Adverse perinatal outcomes
- Multiple gestations
- Structural congenital abnormalities
- Chromosomal abnormalities
- Imprinting disorders

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Searches of Unpublished Data

Description of Methods Used to Collect/Select the Evidence

Published literature was retrieved through searches of Ovid MEDLINE and the Cochrane Library for English-language articles related to assisted reproduction and perinatal outcomes published from January 2005 to December 2012 (overlapping with the previous Society of Obstetricians and Gynaecologists of Canada guideline) using appropriate controlled vocabulary and key words (assisted reproduction, assisted reproductive technology, ovulation induction, intracytoplasmic sperm injection, embryo transfer, and in vitro fertilization). Results were not restricted to systematic reviews, randomized control trials/controlled clinical trials, and observational studies; studies of all designs published in English from January 2005 to December 2012 were reviewed, and additional publications were identified from the bibliographies of these articles. Well-conducted randomized controlled trials were considered evidence of the highest quality, followed by cohort studies. Searches were updated on a regular basis and incorporated in the guideline to August 2013. Grey (unpublished) literature was identified through searching the websites of health technology assessment and health technology assessment-related agencies, clinical practice guideline collections, clinical trial registries, and national and international medical specialty societies.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Quality of Evidence Assessment*

I: Evidence obtained from at least one properly randomized controlled trial

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II-3: Evidence obtained from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of treatment with penicillin in the 1940s) could also be included in this category

III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees

*Adapted from the Evaluation of Evidence criteria described in the Canadian Task Force on Preventive Health Care.

Methods Used to Analyze the Evidence

Systematic Review

Description of the Methods Used to Analyze the Evidence

The quality of evidence in this document was rated using the criteria described in the Report of the Canadian Task Force on Preventive Health Care (see the "Rating Scheme for the Strength of the Evidence" field).

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Not stated

Rating Scheme for the Strength of the Recommendations

Classification of Recommendations†

A. There is good evidence to recommend the clinical preventive action

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Cost Analysis

The potential impact of a policy of elective single embryo transfer (eSET) in appropriately selected women on perinatal and maternal outcomes is significant, and such a policy could result in substantial cost savings. One modelling study examined the cost utility of this policy, and a multi-centre cohort examining the long-term effects and cost implications of the Dutch policy of eSET is ongoing.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

This clinical practice guideline has been prepared by the Genetics Committee, reviewed by the Reproductive Endocrinology and Infertility Committee and the Family Physicians Advisory Committee, and approved by the Executive and Council of the Society of Obstetricians and Gynaecologists of Canada.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- Appropriate obstetrical management and counseling of prospective parents regarding assisted human reproduction (AHR) procedures
- Clinicians who are better informed about the adverse effects that have been documented in association with AHR

Potential Harms

Not stated

Qualifying Statements

Qualifying Statements

This document reflects emerging clinical and scientific advances on the date issued and is subject to change. The information should not be construed as dictating an exclusive course of treatment or procedure to be followed. Local institutions can dictate amendments to these opinions. They should be well documented if modified at the local level. None of these contents may be reproduced in any form without prior written permission of the Society of Obstetricians and Gynaecologists of Canada (SOGC).

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Foreign Language Translations

For information about availability, see the *Availability of Companion Documents and Patient Resources* fields below.

Categories

IOM Care Need

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

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Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2006 Mar (revised 2014 Jan)

Guideline Developer(s)

Society of Obstetricians and Gynaecologists of Canada - Medical Specialty Society

Source(s) of Funding

Society of Obstetricians and Gynaecologists of Canada (SOGC)

Guideline Committee

Genetics Committee

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Financial Disclosures/Conflicts of Interest

Disclosure statements have been received from all contributors.

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Guideline Availability

Electronic copies: Available from the [Society of Obstetricians and Gynaecologists of Canada \(SOGC\) Web site](#) . Also available in French from the [SOGC Web site](#) .

Print copies: Available from the Society of Obstetricians and Gynaecologists of Canada, La société des obstétriciens et gynécologues du Canada (SOGC) 780 promenade Echo Drive Ottawa, ON K1S 5R7 (Canada); Phone: 1-800-561-2416.

Availability of Companion Documents

None available

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on May 7, 2014. The information was verified by the guideline developer on June 4, 2014.

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